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DENTATE GRANULE CELLS FORM NOVEL BASAL DENDRITES IN A RAT MODEL OF TEMPORAL LOBE EPILEPSY

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Abstract—Mossy fibre sprouting and re-organization in the inner molecular layer of the dentate gyrus is a characteristic of many models of temporal lobe epilepsy including that induced by perforant-path stimulation. However, neuroplastic changes on the dendrites of granule cells have been less-well studied. Basal dendrites are a transient morphological feature of rodent granule cells during development. The goal of the present study was to examine whether granule cell basal dendrites are generated in rats with epilepsy induced by perforant-path stimulation. Adult Wistar rats were stimulated for 24 h at 2 Hz and with intermittent (1/min) trains (10 s duration) of single stimuli at 20 Hz (20 V, 0.1 ms) delivered 1/min via an electrode placed in the angular bundle. The brains of these experimental rats and age- and litter-matched control animals were processed for the rapid Golgi method. All rats with perforant-path stimulation displayed basal dendrites on many Golgi-impregnated granule cells. These basal dendrites mainly originated from their somata at the hilar side and then extended into the hilus. Quantitative analysis of more than 800 granule cells in the experimental and matched control brains showed that 6–15% (mean=8.7%) of the impregnated granule cells have spiny basal dendrites on the stimulated side, as well as the contralateral side (mean=3.1%, range=2.9–3.9%) of experimental rats, whereas no basal dendrites were observed in the dentate gyrus from control animals.

The formation of basal dendrites appears to be an adaptive morphological change for granule cells in addition to the previously described mossy fibre sprouting, as well as dendritic and somatic spine formation observed in the dentate gyrus of animal and human epileptic brains. The presence of these dendrites in the subgranular region of the hilus suggests that they may be postsynaptic targets of the mossy fibre collaterals. © 1998 IBRO. Published by Elsevier Science Ltd.

Key words: perforant-path stimulation, basal dendrites, mossy fibre, sprouting, dentate gyrus, rat.

The kainate and pilocarpine animal models of status epilepticus (SE) produce widespread brain damage and the delayed occurrence of limbic and generalized convulsions.[8,9] Electrical stimulation of the perforant-path under urethane anaesthesia in adult rats produces neuronal injury which is restricted to the hippocampus, has an excitotoxic appearance similar to that induced by kainic acid[27,29,42,45] and is associated with a loss of frequency-dependent, paired-pulse inhibition in the dentate gyrus,[43] as well as the progressive development of spontaneous recurrent seizures.[41] The type of hippocampal damage that is seen in animal models of SE is remarkably similar to that seen in human patients with temporal lobe epilepsy.[11,15,19] Spontaneous seizures have been tentatively explained either by the sprouting and re-organization of recurrent excitatory connections[1,9,10,49,50,53] or by the loss[26] or deafferentation[4,43] of inhibitory interneurons in the hippocampus.

The sprouting of granule cell axons, the mossy fibres, is commonly inferred in the dentate gyrus of humans and experimental animals with epilepsy. In the affected hippocampal formation, sprouted mossy fibres form an aberrant band in the inner molecular layer of the dentate gyrus where they are in position to synapse with the proximal apical dendrites of granule cells.[11,15,31,50,53] The elements postsynaptic to the mossy fibres also display changes in temporal lobe epilepsy. For example, kainic acid treatment in adult mice results in dendritic hypertrophy with

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Abbreviations: ISI, interstimulus interval; PB, phosphate buffer; PS, population spike; SE, status epilepticus.

increased numbers of dendritic spines that is correlated with the sprouting of mossy fibres.[52] In human studies, a greater density of dendritic spines was noted in granule cells that exhibited aberrant mossy fibre collaterals as compared to cells without such collaterals.[16] In another study, longer and more branched granule cell apical dendrites were found in tissue from patients with mesial temporal lobe sclerosis as compared to those from a control group.[54] Associated with the seizure-induced changes in granule cells are molecular responses that include increases in mRNAs encoding various neurotrophic substances.[13] These latter changes are often reminiscent of developmental processes.

The granule cells of adult rats lack basal dendrites, although they are transiently expressed in rats during postnatal development.[37,38,40,57] This transient expression is also observed in several other species, including mouse, rabbit, guinea-pigs and cats (see Ref. 37). In contrast, basal dendrites are normal features of granule cells in the developing and adult dentate gyrus of monkeys and humans.[37] The biological significance of the developmental appearance and subsequent attrition of granule cell basal dendrites in rats is unknown. In a recent study, Franck *et al.*[12] remarked on the apparent high spine density on the basal dendrites of granule cells in the brains of adult epileptic humans and suggested that their occurrence may provide an additional basis for recurrent excitation. However, no comparison was made with the basal dendrites of age-matched humans and therefore it is unclear whether these basal dendrites are within the normal range observed in humans.[37]

The present study aimed to determine whether basal dendrites appear on granule cells of adult rats as a consequence of SE induced by perforant-path stimulation. Such an analysis conducted in epileptic rats would provide novel information about the formation of dendrites in the epileptic brain because, unlike humans, normal adult rats lack basal dendrites. A rapid Golgi method was used to assess the dendritic arbors of granule cells. A preliminary report of the data has been published in abstract form.[33]

EXPERIMENTAL PROCEDURES

Surgery

Male adult Wistar rats (400–500 g; Simonsen Labs) were injected with ketamine (50 mg/kg) and xylazine (10 mg/kg). At 30 min after injection animals were placed in a stereotactic apparatus. Rectal temperature was monitored continuously and maintained at 37 ± 0.5°C with a warm water coil placed under the animal during anaesthesia. Two holes were drilled on the left side of the skull to accommodate the stimulating and recording electrodes. The stimulating electrode was 1 mm anterior and 4.5 mm lateral to lambda, and that for the recording electrode was 3.0 mm anterior and 2.2 mm lateral to lambda. Four jeweller's screws (two anterior, one right, one posterior) were also placed into pre-drilled holes on the right side of the skull. Bipolar electrodes made of twisted Teflon-coated 0.005 inch diameter stainless steel wires (California Fine Wire Co.; tip separation <1 mm for recording electrodes and <0.5 mm for the stimulating electrodes) were cemented to the skull by dental acrylate. Final electrode depth (2.5–3.5 mm from cortical surface) was determined by maximizing the amplitude of the characteristic potential recorded in the dentate gyrus in response to ipsilateral perforant-path stimulation. Chromium non-coated wires (Consolidated Wire and Associated Co.) were connected to the screws on the skull and used as ground electrodes. The skin was cleaned with Povidine solution (Rugby Laboratories) and 10 mg of penicillin (Sigma) was injected subcutaneously once per day for three days after surgery.

In vivo recordings

Input/output (I/O) responses were obtained at 125, 200, 300, 500, 700, 1000, 2000 and 3000 μA (0.1 Hz, 0.2 ms duration, biphasic stimulation). Interstimulus interval (ISI)-dependent paired-pulse responses were studied at intervals of 40 and 400 ms (0.1 Hz, 0.1 ms duration, monophasic stimulation). Population spike (PS) amplitudes were measured from the average of five consecutive evoked potentials. PS amplitude was calculated as [(field potential at the beginning of PS)+(field potential at the end of PS)]/2 − (field potential at the peak of PS). In multiple PS discharges, we used the first PS to measure PS amplitude. The inhibition score in paired-pulse examinations was calculated as [100 − (PS amplitude of second pulse)/(PS amplitude of the 1st pulse) × 100].

Perforant-path stimulation

One to two weeks after surgery, rats were anaesthetized with a loading dose of urethane (1000 mg/kg) via the tail vein followed by a continuous infusion at 0.08 ml/min (1200 mg/kg). Once anaesthetized, rats were then stimulated for 22–24 h with single stimuli (20 V, 0.1 ms duration) at 2 Hz and with intermittent trains (10 s duration) of stimuli at 20 Hz delivered once per minute to the implanted stimulating electrode. Paired-pulse stimulation was carried out before, during and at various times after stimulation. One hour after the end of stimulation animals were injected with furosemide (10 mg/kg, i.m.). At various times rats were also injected subcutaneously with small volumes of dextrose solution.

Neurobiotin detection in granule cells

Intracellular recordings were made in hippocampal slices (400 μm-thick) from stimulated and control rats according to previously described methods.[56] Intracellular microelectrodes contained 1.5% Neurobiotin in 3 M potassium acetate (pH=7.25). Neurobiotin was injected into granule cells (one cell/slice) using square-wave current pulses (1–3 nA, 100 ms, 3 Hz) for 15 to 25 min. Slices were immersed overnight in 4% paraformaldehyde in 0.1 M phosphate buffer (PB, pH=7.4). Slices were then incubated in 0.1 M PB containing 1% avidin–biotin–peroxidase complex (ABC; Vector) and 0.2% Triton X-100 at 4°C for 48 h. The Neurobiotin labelling was visualized in 0.05% diaminobenzidine and 0.005% H_2O_2 in PB. The reaction was stopped by washing slices with PB.

Golgi method

Three months after perforant-path stimulation, the experimental rats and their age- and litter-matched controls were anaesthetized with an overdose of pentobarbital (60 mg/kg) and perfused intracardially with cold saline followed by 4% paraformaldehyde and 0.5% glutaraldehyde in 0.1 M PB. The brain was removed and placed overnight in the perfusion fixative at 4°C. The caudal cerebrum containing the hippocampal formation was blocked into 3 mm-thick slices that were processed with a modified rapid Golgi method. Briefly, blocks from experimental and control brains were

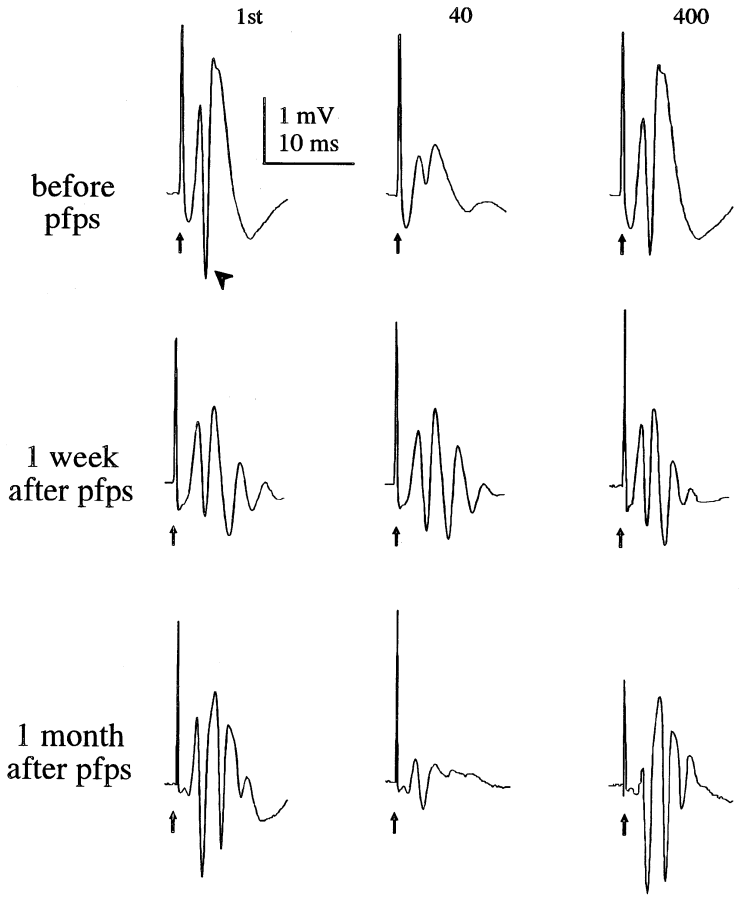

Fig. 1. Changes in paired-pulse inhibition after perforant-path stimulation (pfps). (A) *In vivo* recording traces from a rat before and after perforant-path stimulation. The traces are averages of five consecutive waveforms. Arrows note the onset of the perforant path stimulus (0.1 ms, 30 V monophasic). The first upward deflection after the stimulus artifact in each trace is the field excitatory postsynaptic potential followed by a population spike discharge (arrowhead in first trace). In each set of traces, the left trace is the response to the 1st stimulus of a paired-pulse, middle trace the response to the 2nd stimulus at 40 ms ISI, and the right trace the response to the 2nd stimulus at 400 ms ISI. Note the multiple population spike discharges after perforant-path stimulation. Also note the recovery of the 40 ms ISI inhibition and the lack of recovery in the 400 ms ISI paired-pulse inhibition.

immersed in a freshly made solution of osmium tetroxide (0.25%) and potassium dichromate (9%) for five days in the dark. The blocks were then rinsed several times with 0.75% silver nitrate and placed in this latter solution for two days in darkness. Brain blocks were blotted dry with tissue paper and sectioned at 70 μm. The sections were dehydrated in a graded series of ethanol followed by xylene. Finally, sections were placed on glass slides, and coverslips applied with mounting medium.

Morphometric analysis

Five to 20 sections from each brain were used for quantitative analysis of Golgi-impregnated granule cells. The granule cell layer was scanned with 40× and 100× objectives. Thus, each examined granule cell body was carefully viewed at two high magnifications to determine the continuity of processes in its vicinity. By carefully adjusting the fine focus, it was possible to determine whether a basal dendrite was present and to distinguish a passing dendrite from one that was attached to the examined cell body. Data were collected separately for the two hemispheres and the total number of examined granule cells and the percentage of those with basal dendrites were calculated. Camera lucida drawings of Golgi-impregnated granule cells from control and stimulated rats were made using a 100× oil objective to illustrate the pattern of dendrites and axonal branching. Images were obtained with a digital video camera and a light microscope, and montages of impregnated granule cells at different focal planes were made using a UMAX Supermac computer and Adobe Photoshop software.

RESULTS

Electrophysiology

In paired-pulse recordings, the short (40 ms) and long (400 ms) ISI-dependent inhibition were greatly depressed during the 1st week following perforant-path stimulation (compare top and middle traces in Fig. 1). At four weeks after perforant-path stimulation, short ISI-dependent inhibition, which is thought to be $GABA_A$ receptor-mediated,[44] appeared to recover (bottom traces in Fig. 1). Long ISI-dependent inhibition, in contrast, did not recover

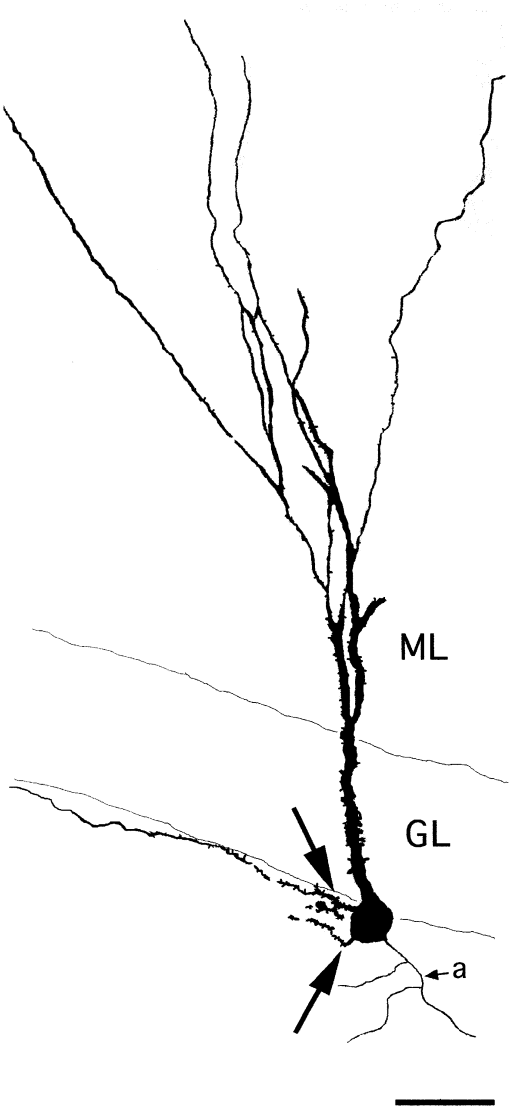

Fig. 2. Camera lucida drawing of a Neurobiotin-filled granule cell from a perforant-path-stimulated rat. Note the presence of basal dendrites (large arrows) and an axon (a and small arrow) that arise from soma of this cell. Spines are present on the surface of the basal dendrites and their branches. The granule cell layer is indicated by the pair of parallel lines. Scale bar=20 μm. ML, molecular layer; GL, granule cell layer.

and remained suppressed at four weeks after perforant-path stimulation. The multiple PS discharges which were never observed prior to perforant-path stimulation also persisted at four weeks after perforant-path stimulation. These results confirmed our previous findings of persistent hyperexcitability in the rat dentate gyrus at one month after perforant-path stimulation.[41,47]

Based on our results from evoked potential recordings we decided to explore the possible mechanisms which underlie chronic hyperexcitability with the use of intracellular recording techniques. Specifically, we focused attention on animals at one month after stimulation, a time at which rats were previously reported to exhibit spontaneous seizures and accelerated kindling.[41,56] Our initial aim was to characterize the possible differences in the membrane properties and synaptic responses of granule cells in hippocampal slices taken from control animals and from experimental rats subjected to perforant-path stimulation. A description of the intracellular recording results is the subject of a separate manuscript (Spigelman *et al.*, unpublished observations). During these recordings, granule cells in slices obtained from stimulated and control rats were injected with Neurobiotin tracer and processed for morphological identification. In one of the neurons from the stimulated group, we noted the presence of a large basal dendrite which ran parallel to the granule cell layer and partly extended into the hilar region (Fig. 2).

Since basal dendrites are normally absent in adult rats this warranted further investigation. To this end, we implanted electrodes and stimulated several additional rats and used the rapid Golgi method to study the morphology of granule cells in these rats and their age-matched non-stimulated, but implanted controls. Others have demonstrated that the re-organization of circuits in the dentate gyrus after seizures is a time-dependent process which reaches a plateau by 100 days.[22,25] Therefore, we chose to study the morphology of granule cells at three months after perforant-path stimulation to allow sufficient time for the morphological changes to occur.

Morphology of granule cells in non-stimulated control adult rats

In Golgi preparations, granule cells in the dentate gyrus were easily identified according to their characteristic soma location and dendritic morphology. Granule cell bodies were round or oval shapes with their greater diameter oriented perpendicular to the granule cell layer. A granule cell typically gave rise to an apical dendrite that extended into and arborized within the molecular layer (Fig. 3A). The axons of granule cells originated from the hilar pole of the soma and projected into the hilus. Consistent with earlier Golgi studies in this brain region, our data showed that granule cells from control adult rats have no thick processes arising from the hilar side of their somata that could be interpreted as basal dendrites (Fig. 3A).

Morphology of granule cells in stimulated rats

In general, the appearance of granule cell bodies and the arborization pattern of their apical dendrites within the molecular layer of the dentate gyrus in perforant-path stimulation rats were similar to those of the control group. Furthermore, axons of granule cells arose from their hilar pole.

A consistent morphological difference in granule cells from the stimulated rats was the presence of a distinct basal dendrite on many of these cells. These basal dendrites most frequently arose from the hilar pole of granule cell bodies, and were distinctly separated from the axons of these cells (Figs 3B, 4, 5). Basal dendrites were less commonly seen to originate from the lateral sides of granule cell somata and from the base of the apical dendrites (e.g., Figs 4F and 6). Some granule cells only gave rise to a single basal dendrite but it would extend into the hilus for various lengths, usually 200–500 μm, whereas other granule cells had basal dendrites that branched. However, in all cases, the basal dendrites were restricted to the subgranular region of the hilus that was previously defined as the first 50 μm subjacent to the granule cell layer.[32] Figure 4 illustrates some of the different morphologies of the encountered basal dendrites. It should also be noted that the axons of granule cells from stimulated rats were frequently observed to send collaterals through the granule cell layer into the inner molecular layer (Fig. 4D, F), indicating mossy fibre sprouting and re-organization. The diameter of basal dendrites could be as thick as that of the apical dendrite which arose from the opposite pole of a given granule cell (e.g., Figs 3B and 5A–C). Basal dendrites had few branches (range 0–5), and the branch length varied from 20–200 μm. Densely packed spines were present on the surface of the basal dendrites and their branches throughout their length (Figs 3–6).

Quantitative analysis of basal dendrites

Due to the technical limitations of the Golgi method, the number of impregnated granule cells varied in a given coronal section from any brain, ranging from 2–40 cells per section. Three matched pairs of control and stimulated brains were well-stained, whereas the 4th pair of brains was sub-optimally impregnated, such that only a small number of granule cells were labelled on the left (electrode-implanted) hemisphere. Altogether, five to 20 sections in each brain were analysed for quantification so that the number of impregnated granule cells studied ranged from 13–536 for each cerebral hemisphere. Table 1 summarizes the results of granule cell counts in the brains of stimulated rats and the implanted controls. Quantitative analysis of more than 1700 granule cells in the four pairs of experimental and control brains showed that 8.7% (76/874) of Golgi-impregnated granule cells have spiny basal dendrites on the stimulated side of experimental rats, whereas no basal dendrites were observed in the dentate gyrus from control animals (0/889). Basal dendrites were found in hippocampi from both hemispheres, however a higher prevalence of basal dendrites was seen on the stimulated (left) side than on the contralateral side (mean=3.1%, 12/386, n=3 brains).

DISCUSSION

The present study provides the first description of the formation of granule cell basal dendrites in a rat model of temporal lobe epilepsy induced by perforant-path stimulation. The frequency of basal dendrites for granule cells was quantified, and such dendrites are consistently found in the dentate gyrus of epileptic rats. The finding of granule cell basal dendrites is of considerable interest because, as suggested by earlier studies and confirmed in the current investigation, the granule cells in normal adult rats do not possess basal dendrites.[37,38] Further, it is significant to note that basal dendrites appear only transiently during normal development of the rat.[38] Thus, the presence of basal dendrites in adult

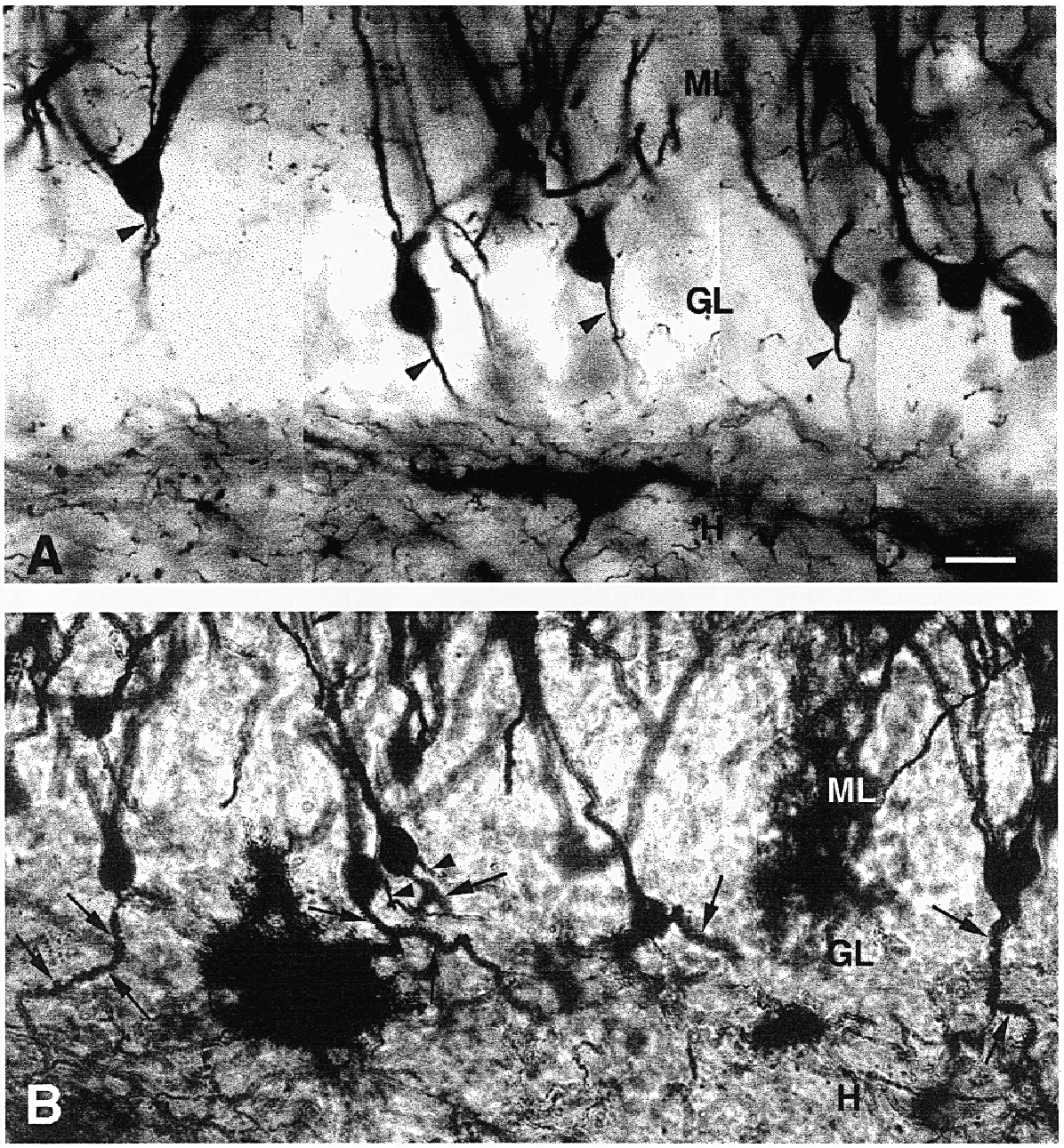

Fig. 3. Low magnification of the dentate gyrus in control (A) and perforant-path-stimulated rats illustrating the axons (arrowheads) emerging from the base of control granule cells in A, and basal dendrites (arrows) at the base of the cells from a stimulated rat in B. Scale bar=10 μm. ML, molecular layer; GL, granule cell layer; H, hilus.

epileptic rats suggests a neuronal response to seizures that may be related to the generation of new granule cells (see below).

It should be noted that the present study is not the first to illustrate granule cell basal dendrites in the epileptic dentate gyrus of adult rodents. However, it is the first to describe them. For example, in a previous Golgi study of adult Wistar rats treated with kainic acid, basal dendrites appear to be present on one of several illustrated dentate granule cells (see Fig. 3C, D in Ref. 30). In a more recent study of this model of epilepsy in adult mice, granule cells were labelled with biocytin and one of the illustrated cells apparently possesses a basal dendrite (see Fig. 1B in Ref. 52). In contrast, illustrated granule cells from control animals in these two reports did not have basal dendrites. However, neither study provided a description of these basal dendrites. Nevertheless, these observations, taken together with the present data, suggest

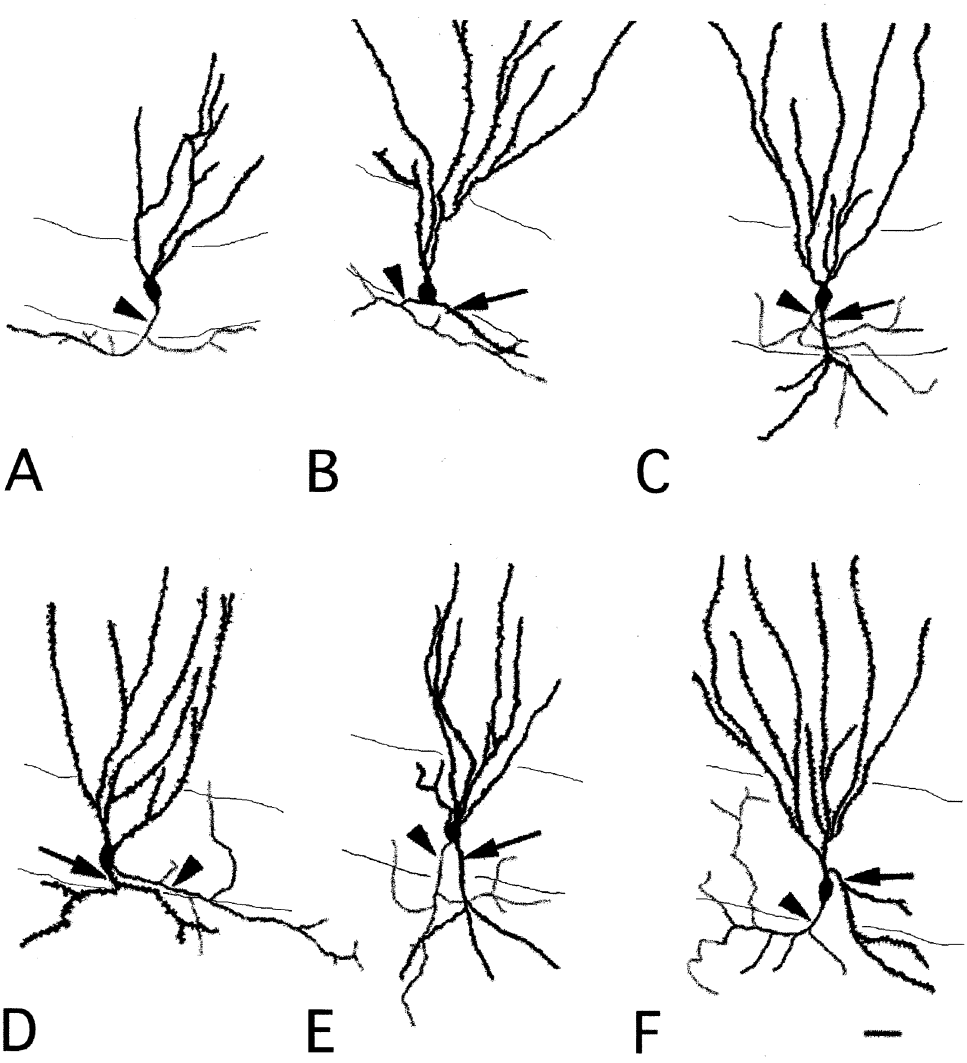

Fig. 4. Camera lucida drawings of Golgi-impregnated granule cells from control (A) and perforant-path-stimulated rats (B–F). Granule cell axons are indicated with arrowheads and basal dendrites with arrows. The granule cell layer is indicated by the pair of parallel lines. Scale bar=10 μm.

that the formation of basal dendrites may be a common response of rodent hippocampal granule cells to seizures.

Formation of novel basal dendrites observed in the present model of temporal lobe epilepsy may represent one of the adaptive cellular changes of the granule cells in response to epileptogenic stimuli. It has been shown that, following intrahippocampal administration of kainic acid, modifications of neuronal structures involve virtually all cellular compartments. For example, granule cells exhibit dramatic hypertrophy that is associated with altered expression of various neurotrophins.[14,18,24,51] Hypertrophy of the axonal compartment consists of mossy fibre sprouting, which has been the most commonly recognized structural modification of the granule cells.[11,15,21,23,24,31,40,48,50,53] Hypertrophic changes are also observed on the soma and apical dendrites of granule cells. These include increases of dendritic size and length, and spine density on both somata and dendrites.[6,51] Thus, formation of basal dendrites observed in the present and other models of temporal lobe epilepsy could account for an additional form of dendritic neuroplasticity of granule cells.

New granule cells continue to be generated in the rodent dentate gyrus throughout adult life.[3,17] Therefore, basal dendrites could arise from granule cells generated after SE, as opposed to sprouting of basal dendrites from mature cells generated prior to SE. Recently, granule cells generated *de novo* after pilocarpine- or perforant-path stimulation-induced SE were shown to project aberrant mossy fibre collaterals into the inner molecular layer of the dentate gyrus.[28] We observed granule cell somata with basal dendrites both at the outer (molecular layer) edge of the granule cell layer, as well as at the

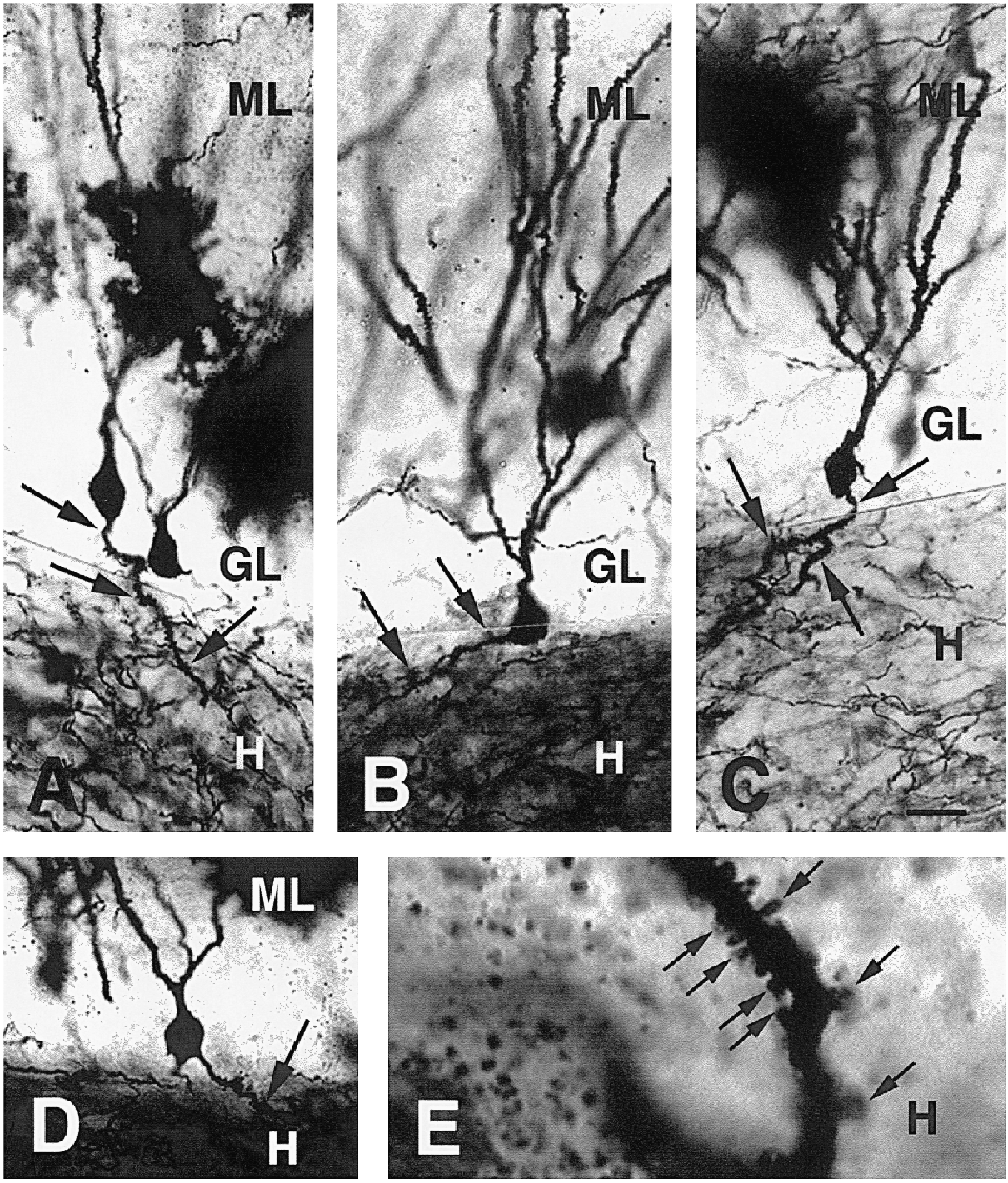

Fig. 5. Detailed images of individual granule cells from different experimental rats to show the variability in the morphology of basal dendrites. (A, B, C, D) have cells with basal dendrites that are indicated by arrows. (E) is an enlargement of a portion of the basal dendrite in A to show its dendritic spines (arrows). Scale bar in C (10 μm) applies to A–D. Scale bar for E=2.5 μm.

hilar edge. Based on normal neurogenesis and migration patterns,[7,20] basal dendrite-possessing granule cells with somata located at the molecular layer edge would be expected to be generated prior to SE. However, recent observations indicate that granule cells generated after SE do not follow normal migration patterns, resulting in ectopic locations of the newly differentiated cells both in the hilus and in the inner molecular layer.[28] Thus, cells with basal dendrites may represent post-SE generated granule cells,

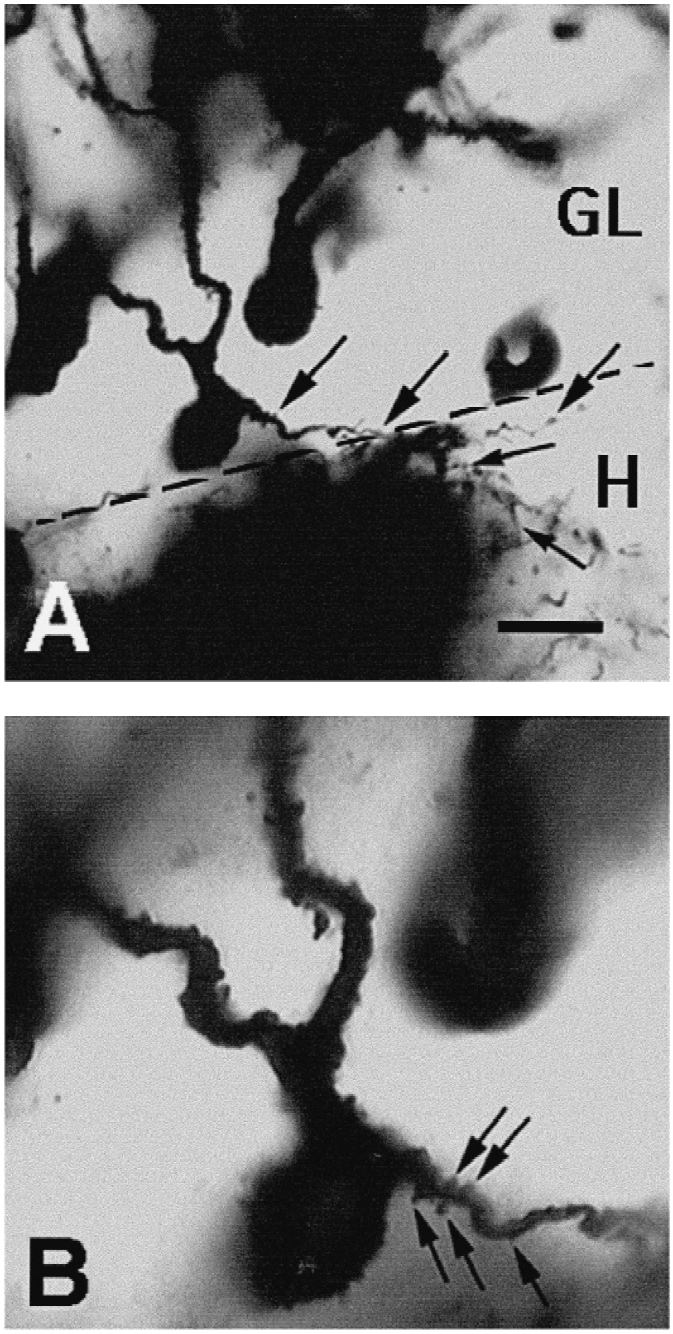

Fig. 6. Example of a granule cell that formed a basal dendrite from its molecular layer pole close to the origin of the apical dendrite. The basal dendrite extends and branches (arrows) into the subgranular zone of the hilus (A). (B) is an enlargement illustrating the presence of dendritic spines (arrows) on the basal dendrite, as well as on the soma and apical dendrites of this granule cell. Scale bars in A and B are 15 and 8 μm, respectively. ML, molecular layer; GL, granule cell layer. Broken line in A indicates the border of GL and hilus.

or they may represent pre-existing mature cells with sprouted basal dendrites, or a combination of the two.

The cause and biological significance of basal dendrite generation in granule cells after SE are unclear, though, they may be generally similar to other adaptive cellular processes that occur in the epileptic hippocampal formation. For example, perforant-path stimulation initiates excitotoxicity that causes neuronal injury and death in the hippocampal formation, especially, the hilar region.[27,42,45,56] Expression of neurotrophins such as nerve growth factor is altered within hours and these changes persist for months following a kainic

Table 1. Incidence of basal dendrites in stimulated and control rats

Rat no.	Left hemisphere granule cells			Right hemisphere granule cells		
	Cells with basal dendrites	Total cells counted	% of cells with basal dendrites	Cells with basal dendrites	Total cells counted	% of cells with basal dendrites
Stimulated 1	51	536	9.5	8	266	3
Stimulated 2	13	210	6.2	2	51	3.9
Stimulated 3	10	115	8.7	2	69	2.9
Stimulated 4	2	13	15	—	—	—
Control 1	0	510	0	—	—	—
Control 2	0	200	0	—	—	—
Control 3	0	156	0	—	—	—
Control 4	0	23	0	—	—	—

acid-induced hippocampal lesion.[14,51,52] These growth factors appear to trigger structural remodelling and bring granule cells back to infancy when basal dendrites are present.[38,39] Additionally, dendritic plasticity, especially spine formation or regression, can be linked to changed numbers of putative presynaptic elements during the development and regeneration processes.[5] It was suggested that hypertrophy of dendritic spines in the kainate model of epilepsy depends on the presence and functional activity of sprouted mossy fibres.[30,52] The result of the basal dendrite formation may be to produce additional recurrent excitatory circuits in the dentate gyrus of the epileptic brain. Mossy fibres are found normally in the subgranular region. One possibility is that the loss of hilar neurons and their dendrites in the subgranular zone acts as a catalyst for granule cells to sprout their dendrites into this region to replace a major postsynaptic target of mossy fibres. Dendritic spines are well known to possess glutamatergic receptors and are contacted by axon terminals that form asymetric synapses.[2] Therefore, the presence of spines on the basal dendrites is strongly suggestive of excitatory presynaptic inputs. It is also possible that the newly formed basal dendrites may receive innervation not only from the mossy fibres but also from other sprouted inputs which normally impinge on hilar neurons. For example, the vulnerable mossy cells in the hilar region are known to receive functional GABAergic innervation.[34,46] With the loss of mossy cells the surviving inhibitory GABAergic interneurons could seek new targets and innervate the newly formed basal dendrites of granule cells. It would be interesting to identify the presynaptic elements of the granule cell basal dendrites so we can begin to understand their role in epileptic states.

CONCLUSION

Although basal dendrites were initially suggested that represent a pathological feature of granule cells in the brains of patients with temporal lobe epilepsy,[35] they were later found to be present in the dentate gyrus of normal adult primates.[36,37] However, the number of granule cells that possess basal dendrites in the epileptic human dentate gyrus (43% of 246 granule cells from Ref. 55) appears to be greater than in normal human dentate gyrus (22% of 392 granule cells from Ref. 37). The observation of mossy fibre contacts on basal dendrites in human epileptic tissue suggests a substrate for recurrent excitation of granule cells.[12] The perforant-path stimulation-induced formation of basal dendrites on rat granule cells underscores the remarkable similarity of this model to human temporal lobe epilepsy and provides a morphological substrate for detailed physiological studies on the role of basal dendrites in temporal lobe epilepsy in a well-controlled experimental system.

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